

REMARKS

Claims 10-14 and 16-18 are pending in the application. Claims 17 and 18 are withdrawn. Claim 15 has been cancelled without prejudice or disclaimer. Support for the amendments to Claim 10 may be found in the specification at page 6, lines 22-23, at page 13, lines 27-29 and at page 16, lines 28-29. Support for the amendment to Claim 17 may be found in the specification at page 6, lines 22-23. No new matter has been added.

The election to prosecute the invention of Group I, Claims 10-16 in the subject application is confirmed. Rejoinder of currently withdrawn Claims 17 and 18 is respectfully requested.

Claims 10-16 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Martini, et al. WO 03/068195 (WO'195) and Lewis, et al. US 2004/0081697 (US'697). Applicants respectfully traverse this rejection.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness and is using hindsight to pick and choose among the various compositions, active ingredients and dosage form elements described in WO'195 and US'697 to support the Section 103 rejection in this case. Applicants further submit that neither WO'195 nor US'697, taken alone, describe or suggest the claimed dosage form and that neither the Examiner, nor the disclosures of WO'195 and US'697, describe or otherwise provide sufficient motivation for one skilled in the art to consider these references in combination.

Examiner contends that it would have been obvious to formulate an erodable core that comprises two compounds - rosiglitazone and another anti-diabetic agent, particularly metformin. However, the claimed oral dosage form comprises more than just an erodable core containing rosiglitazone and metformin.

US'697 discloses several different modified release compositions that provide delayed, sustained and pulsed release. US'697 also discloses compositions comprising rosiglitazone and other antidiabetic agents. Accordingly, significant picking and choosing among the various modified release compositions and anti-diabetic agents disclosed in this reference is required to identify a modified release composition comprised of rosiglitazone and metformin in an erodable core.

The WO'195 publication discloses a sustained release oral dosage form that comprises an erodable core comprising rosiglitazone surrounded by an enteric coating with openings leading to the core. The particular oral dosage formulation described in this reference was designed for delivery of a pharmaceutically active weak base – defined at page 3, lines 4-15 as a base “the conjugate acid of which has a pKa of less than 11.5.” Metformin possesses a pKa of 12.4 (See page 1 of the reference cited on the accompanying IDS). Applicants respectfully submit that the Examiner has provided no reason as to why one skilled in the art would look to the formulation described in WO'195 as suitable or desirable for delivery of a pharmaceutically active base, the conjugate acid of which has a pKa of greater than 11.5.

Moreover, dosage forms containing a therapeutic amount of both rosiglitazone and metformin would contain amounts of metformin that are over 100x greater than the amount of rosiglitazone. Rosiglitazone, generally administered in therapeutic dosages of 2-8 mg, is far more soluble in the acidic conditions of the stomach (around pH 2) than in the near neutral conditions of the upper intestine (greater than pH5). Metformin, on the other hand, is generally administered in therapeutic dosages of 500-1000mg, is soluble over a wide range of physiological pH and has a narrow window of absorption in the upper intestine, with significantly less absorption of metformin occurring in the stomach or lower intestine.

Applicants respectfully submit that neither the Examiner, nor the disclosures of WO'195 and US'697, describe or otherwise provide sufficient motivation for one skilled in the art to pick and choose among the active ingredients and dosage form elements described in these two references to derive the claimed oral dosage form containing a mixture of rosiglitazone and metformin – where the majority mass of such a dosage form is an active ingredient (metformin) that does not possess a pKa of less than 11.5.

Withdrawal of the Section 103 rejection is respectfully requested.

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Group Art Unit No.: 1615

In view of the above amendments and remarks, reconsideration of this application is requested. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned attorney at the number below.

Respectfully submitted,

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